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# THE EFFECT OF MANNITOL ON CEREBRAL WATER AND ELECTROLYTE CONTENTS IN UNILATERAL CAROTID ARTERY LIGATED RATS*

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## SUMMARY

In the rat, the effect of unilateral carotid artery ligation on cerebral water and electroyte contents were investigated. Chemical changes occured mainly in the first 3 hours of carotid ligation duration. $H_2O$ content was not effected by the ligation. No definitive comment was possible on mannitol effect in this model experiment.

## INTRODUCTION

As a part of the other study (2), the effect of unilateral carotid artery ligation, for different time durations, on the distrubition of water, sodium and potassium contents and upon those contents the effect of mannitol were investigated in rats. Unlike the LEVINE preperation, in this study, any additional procedure, i.e., hypoxia, hypotension or postischemic reperfusion, was not used for cerebral hemispheric ischemia. Involved left cerebral hemisphere showed marked swelling but histologically no necrosis was present. Changes in water, sodium and potassium contents were tried to be correlated with histological findings (2, 12, 15, 21).

## MATERIALS AND METHODS

This experiment was carried out in Istanbul DETAM on the adult Wistar type male rats, weighing 200–300 g and divided into 3/6/10/12 hours experimental groups, on the basis of unilateral common carotid artery li-

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gation duration and each group was also further subdivided to PREMANNITOL to serve as control, MANNITOL–30 and MANNITOL–60, both to serve as two different treated groups. Also, additional 8 rats were studied, to use as NORMAL untreated, unligated control group.

Group–1: Left common carotid artery was ligated for 3 hours, in this experimental group, on 24 rats; of these, 8 rats served in the PREMANNITOL control group which received no treatment, the rest 16 rats received mannitol % 20 1 g/kg as an IV bolus through penis vein, 8 of them being decapitated 30 minutes after mannitol infusion to serve MANNITOL–30 and the rest 8 being decapitated 60 minutes after the infusion to serve MANNITOL–60 treated groups.

Groups–2/3/4: In these experimental groups, the duration of left common carotid artery ligation was 6/10/12 hours respectively and the number of rats employed in each group were 24; serving 8 rats in each PREMANNITOL control, MANNITOL–30 and MANNITOL–60 treated groups of the experiment. First group received no treatment, last two groups received mannitol at the same dose of group–1. Treatment with mannitol in each experimental group was always done at the end of scheduled ligation duration whereas the rats in PREMANNITOL control groups were decapitated, without mannitol infusion. All rats in the experiment inspired normal room air spnontaneusly for whole duration. Carotid artery ligations, IV treatments and decapitations were all done under ether anesthesia. No rats died during the experiment.

The only abnormality observed in all rats following both anesthesia and ligation of the carotid artery was right sided weakness for 20–30 minutes, with permanent left sided Horner syndrome.

Brain removal was carried out as quickly as possible, following decapitation and both cerebral hemispheres were inspected for gross pathological changes by naked eyes. Left cerebral hemispehere showed swelling being marked and marked accordingly with the prolonging carotid artery ligation duration of each experimental group.

Left cerebral hemisphere was then dissected to the cortex and white matter (W. Matter) from each of which samples were taken and placed in the known weighed pots. The pots containing brain parts were reweighed for wet tissue weight and placed in an oven for 48 ∓ 2 hours to dry the weighed brain parts at 105 ∓ 5°C. The water content of the cortex and white matter were calculated from the difference in the wet and dry weights.

Dried brain parts were digested with 5 ml 0.75 HNO3 for 24 hours. After centrifugation of the mixture, the supernatant was taken and $Na^+$,$K^+$ ion concentrations were measured with a flame photometer. Ion concentrations were calculated in mEq/kg wet tissue, using–Dilution factor the figure read on the flame photometer for each ion: ; Dilution factor being calculated as 0.75M HNO3 volume/wet weight of the brain part–(in Ref: 18).

Additionally, a group of rats were also studied for the plasma $Na^+$, Urea and glucose level assesments for being able to calculate the plasma osmolality through $2Na^+$ + BUN/2.8 + Glucose/18 formula (22) and also for blood pressure measurements through a cannula in a femoral artery (2) The aim of additional rats usage was because of the withdrawal of blood might change the ion concentrations in the cerebral tissue. Blood samples were taken through tail vein or the cannule in a femoral artery inserted for blood pressure measurements.

## RESULTS

No obvious changes were seen in plasma osmolality and blood pressure levels in both premannitol and postmannitol stages, apart from a minimal rising in blood pressure after mannitol infusion.

*$Na^+$ concentrations:* $Na^+$ concentrations in both W. Matter and Cortex showed a statistically meaningful rise, accordingly with prolonged ligation duration. This trend was similar in both PREMANNITOL control and MANNITOL–30, MANNITOL–60 treated groups (Table–1). Although $Na^+$ concentrations in the experimental groups were lower than the NORMAL one's it raised more or less to normal levels by the 6th. hours of ligation duration which could be explained on the basis of the effectiveness of collateral circulation by the time (Table: 1, Figure: 1,2,3). On the other hand, when, mean values of $Na^+$ concentrations in both W. Matter and Cortex of combined groups were compared each other; it was again obvious that the $Na^+$ concentration falled with carotid artery ligation showed raising back to preligation normal level with the duration of ligation got longer (Table: 5). $Na^+$ concentrations' trend seen in the prolonged carotid artery ligation duration was not changed in the combined PREMANNITOL control, MANNITOL–30 and MANNITOL–60 trated groups.

*$K^+$ concentrations:* As in the $Na^+$ concentrations, $K^+$ concentrations in both W. Matter and Cortex showed statistatically meaningful falling in

Table 1. $Na^+$ Concentrations at different time intervals in 3 subdivided experimental groups. ($Na^+$ in mEq/kg wet tissue)

| Duration of Carotid Artery Ligation | COMPARED SUBDIVIDED GROUPS | | | | | |
|---|---|---|---|---|---|---|
| | Premannitol | | Mannitol-30 | | Mannitol-60 | |
| | W. Matter | Cortex | W. Matter | Cortex | W. Matter | Cortex |
| 3 hours (n: 8) | 37.20 ∓ 3.14 | 40.83 ∓ 8.33 | 26.70 ∓ 2.09 | 60.24 ∓ 8.64 | 20.56 ∓ 7.10 | 22.08 ∓ 2 .16 |
| 6 hours (n: 8) | 61.15 ∓ 4.10 | 70.15 ∓ 3.77 | 76.17 ∓ 11.90 | 80.78 ∓ 8.63 | 63.33 ∓ 4.26 | 64.81 ∓ 4.35 |
| 10 hours (n: 8) | 75.58 ∓ 9.71 | 87.01 ∓ 11.13 | 71.37 ∓ 9.28 | 72.60 ∓ 7.73 | 71.88 ∓ 3.80 | 73.11 ∓ 12.48 |
| 12 hours (n: 8) | 78.71 ∓ 7.08 | 91.26 ∓ 6.58 | 75.29 ∓ 6.01 | 78.38 ∓ 5.95 | 82.54 ∓ 11.91 | 88.61 ∓ 15.79 |
| Kruskal Wallis' Variance Analysis (N: 32) | KW = 24.545 P < 0.01 | KW = 24.480 P < 0.01 | KW = 17.693 P < 0.01 | KW = 16.651 P < 0.01 | KW = 25.057 P < 0.01 | KW = 22.918 O < 0.01 |
| $Na^+$ concentrations in NORMAL rats (n: 8): W. Matter: 73.10 ∓ 7.40 Cortex: 81.65 ∓ 9.91 | | | | | | |

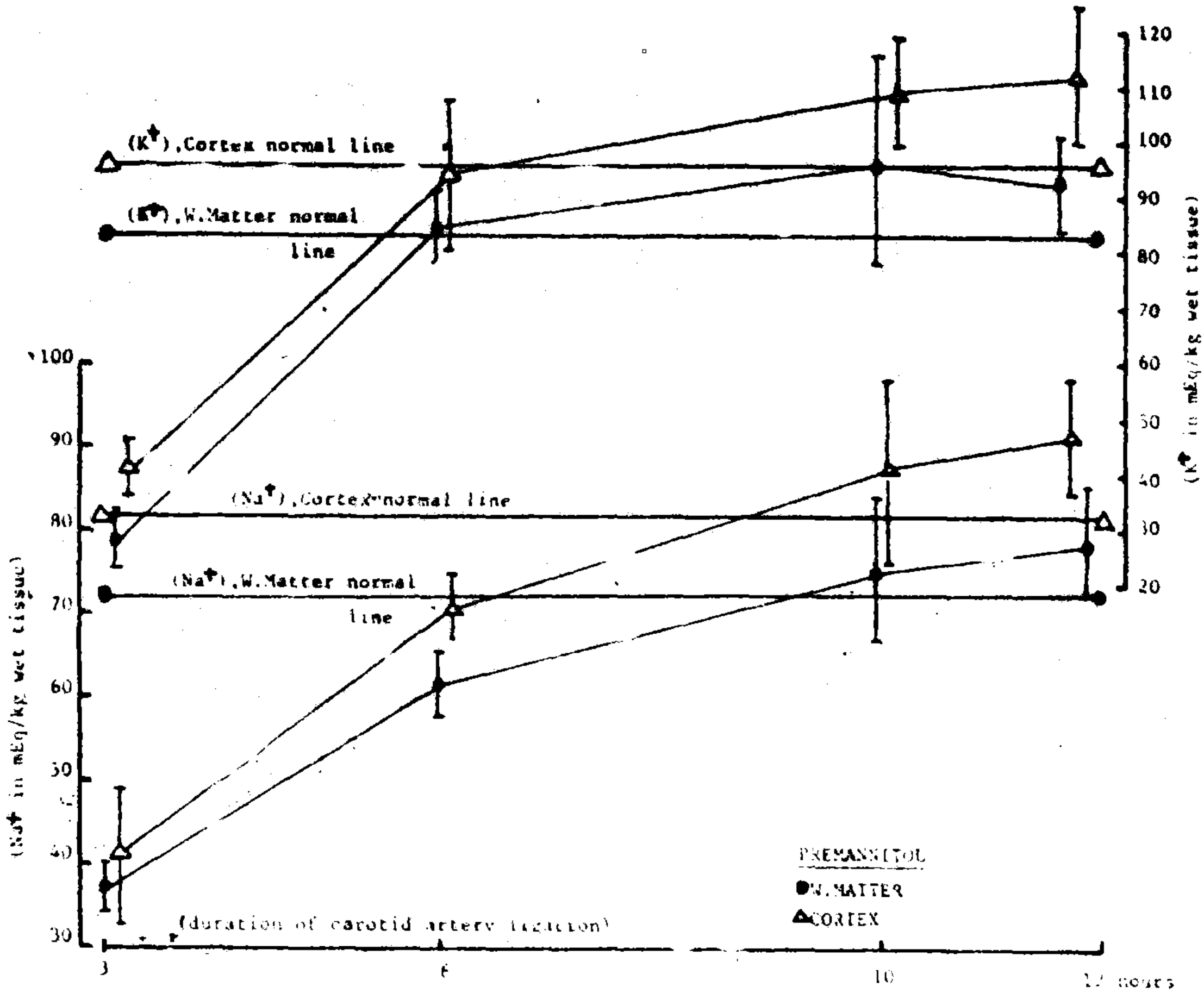


**Figure 1. PREMANNITOL $Na^+$ and $K^+$ concentrations of W. Matter / Cortex versus duration of the ligation.**

the first 6, especially 3, hours of carotid artery ligation duration. It raised to normal levels by the 6 th. hours of carotid ligation. Measurements of $K^+$ concentrations at 10 and 12. th hours of ligation did not showed too much difference than 6. th hours' one. (Table: 2, Figure: 1,2,3). Mean values of $K^+$ concentrations in both W. Matter and Cortex of combined groups are Compared in Table–6 from which it could be seen that the trend related to the duration of carotid artery ligation showed not very important changes in the PREMANNITOL control, MANNITOL–30 and MANNITOL–60 treated groups.

*$Na^+/K^+$ ratios :* This ratio was found to be above 1 in both PREMANNITOL control and MANNITOL–30 and MANNITOL–60 treated groups, especially in the first 3 hours of carotid artery ligation duration. Therefore,

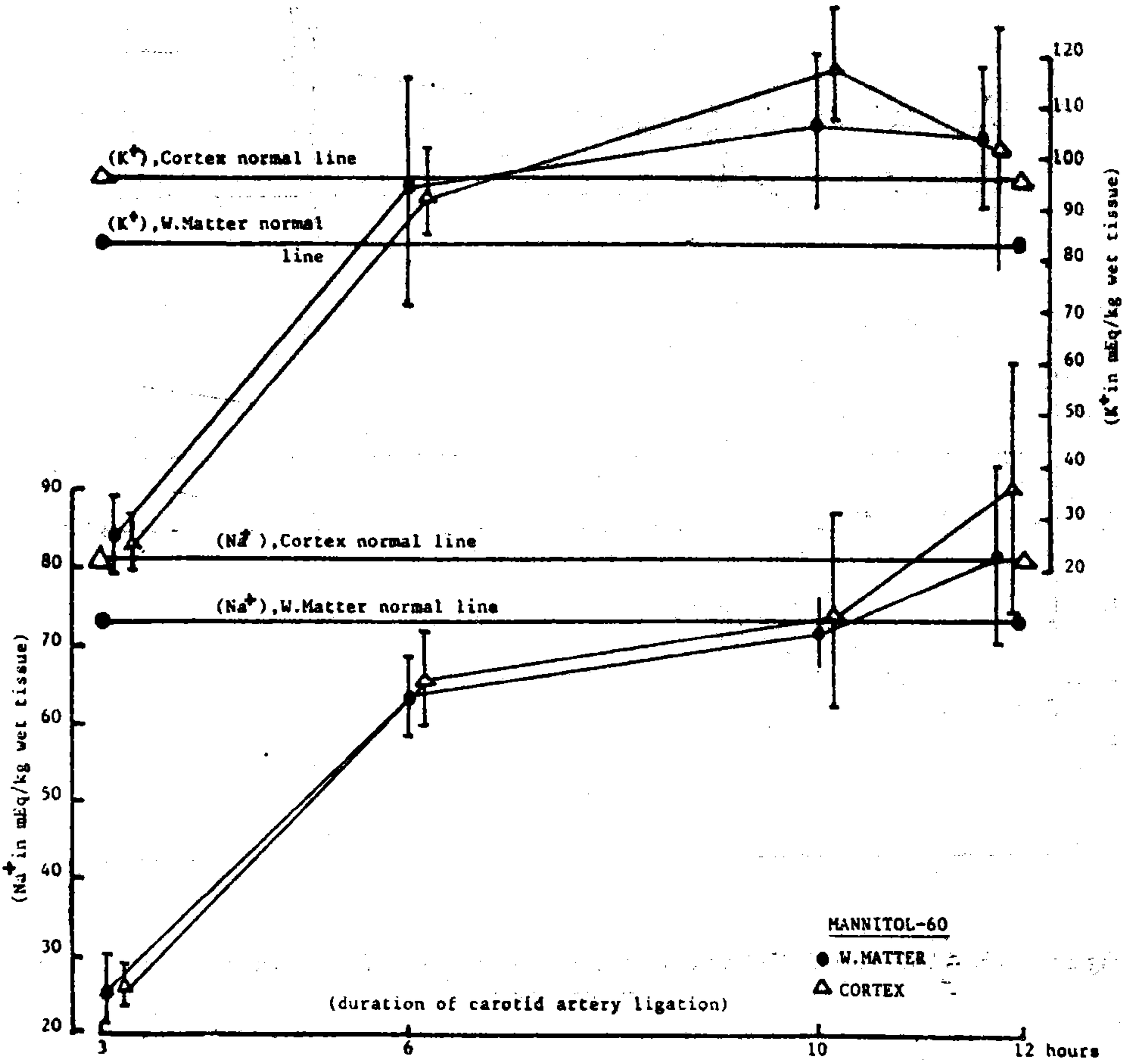


Figure 2. $Na^+$ and $K^+$ concentrations (MANNITOL 30) of W. Matter/ Cortex versus duration of the ligation.

in that period KW values for the W. Matter and Cortex are calculated higher, but it backs to normal from the 6 th. hours of carotid ligation. (Table: 3, 7 Figure: 4).

*$H_2O$ % concentrations:* $H_2O$ concentration of cortex in PREMANNITOL control and MANNITOL–30 treated groups was not affected by the duration of carotid ligation, but in MANNITOL–60 treated group, $H_2O$ concentration of both Cortex and White matter showed meaningful fluctuations, When, $H_2O$ concentrations of Cortex and W. Matter in NORMAL and MANNITOL–30, MANNITOL–60 treated groups were comp-

Table 2. $K^+$ concentrations at different time intervals in 3 subdivided experimental groups. ($K^+$ in mEq/kg wet tissue).

| Duration of Carotid Artery Ligation | COMPARED SUBDIVIDED GROUPS | | | | | |
|---|---|---|---|---|---|---|
| | Premannitol | | Mannitol-30 | | Mannitol-60 | |
| | W. Matter | Cortex | W. Matter | Cortex | W. Matter | Cortex |
| 3 hours (n: 8) | 28.9 ∓ 4.7 | 43.1 ∓ 3.3 | 23.9 ∓ 3.6 | 33.9 ∓ 2.5 | 24. 5 ∓ 5.7 | 20.8 ∓ 2.3 |
| 6 hours (n: 8) | 84.8 ∓ 6.3 | 93.0 ∓ 13.6 | 97.9 ∓ 17.8 | 101.3 ∓ 8.9 | 94. 4 ∓ 21.7 | 93.1 ∓ 7.3 |
| 10 hours (n: 8) | 96.6 ∓ 19.3 | 108.8 ∓ 8.2 | 105.7 ∓ 16.5 | 105.7 ∓ 8.5 | 120. 6 ∓ 10.4 | 117.5 ∓ 10.9 |
| 12 hours (n: 8) | 93.2 ∓ 9.1 | 111.8 ∓ 11.6 | 97.9 ∓ 9.8 | 103.3 ∓ 5.4 | 104.47 ∓ 13.7 | 102.5 ∓ 22.3 |
| Kruskal Wallis' Variance Analysis (N: 32) | KW = 20.815 $P < 0.01$ | KW = 21.804 $P < 0.01$ | KW = 19.321 $P < 0.01$ | KW = 18.284 $P < 0.01$ | KW = 21.554 $P < 0.01$ | KW = 22.413 $P < 0.01$ |
| $K^+$ concentrations in NORMAL rats (n: 8): W. Matter: 82.79 ∓ 10.93 Cortex: 96.11 ∓ 14.33 | | | | | | |

Table 3. $Na^+/K^+$ ratios at different time intervals in 3 subdivided experimental groups.

| Duration of Carotid Artery Ligation | COMPARED SUBDIVIDED GROUPS | | | | | |
|---|---|---|---|---|---|---|
| | Premannitol | | Mannitol-30 | | Mannitol-60 | |
| | W. Matter | Cortex | W. Matter | Cortex | W. Matter | Cortex |
| 3 hours (n: 8) | 1.32 ∓ 0.31 | 0.95 ∓ 0.20 | 1.14 ∓ 0.20 | 1.79 ∓ 0.32 | 0.91 ∓ 0.46 | 1.08 ∓ 0.19 |
| 6 hours (n: 8) | 0.72 ∓ 0.07 | 0.75 ∓ 0.08 | 0.78 ∓ 0.08 | 0.80 ∓ 0.09 | 0.69 ∓ 0.10 | 0.70 ∓ 0.06 |
| 10 hours (n: 8) | 0.82 ∓ 0.11 | 0.80 ∓ 0.11 | 0.68 ∓ 0.07 | 0.69 ∓ 0.08 | 0.67 ∓ 0.03 | 0.62 ∓ 0.10 |
| 12 hours (n: 8) | 0.85 ∓ 0.16 | 0.80 ∓ 0.07 | 0.77 ∓ 0.10 | 0.75 ∓ 0.06 | 0.79 ∓ 0.12 | 0.88 ∓ 0.19 |
| Kruskal Wallis' Variance Analysis (N: 32) | KW = 18.196 $P < 0.01$ | KW = 8.859 $P < 0.05$ | KW = 18.589 $P < 0.01$ | KW = 20.889 $P < 0.01$ | KW = 4.200 $P > 0.05$ | KW = 19.868 $P < 0.01$ |
| $Na^+/K^+$ rations in NORMAL rats (n: 8): W. MATTER: 0.87 ∓ 0.06 CORTEX: 0.85 ∓ 0.10 | | | | | | |

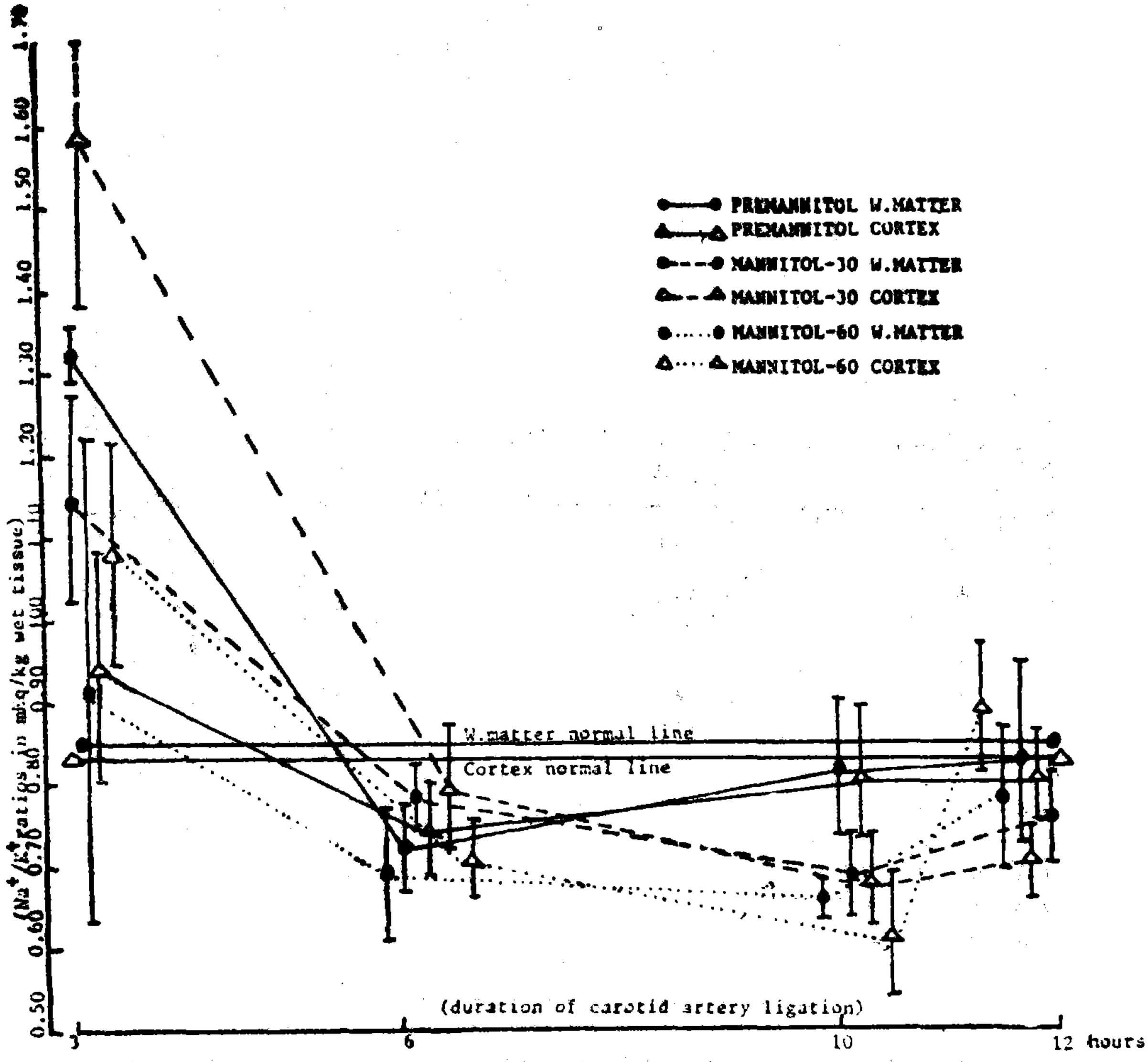


**Figure 3. MANNITOL 60 $Na^+$ and $K^+$ concentrations of W. Matter/ Cortex versus duration of the ligation.**

ared each other, it appears that mannitol lowers the $H_2O$ concentrations in the last two treated groups, but ist was extremely diffucult to make any definite comment in which treated group tit has more antiedematous effect. (Table: 4, 8 Figure: 5).

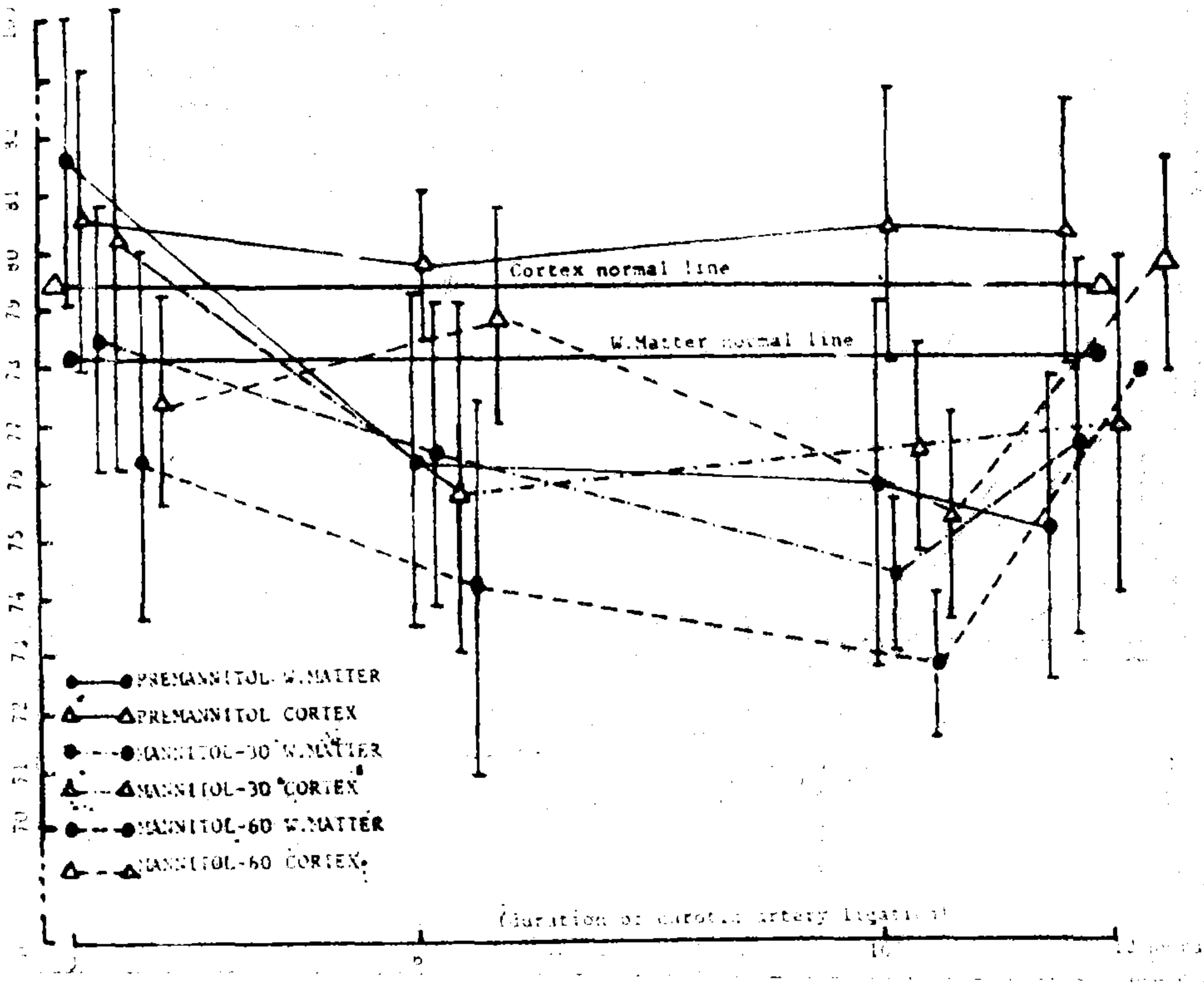


**Figure 4.** $Na^+ / K^+$ ratio trends in 3 subdivided groups, versus duration of the ligation.

Table 4. $H_2O$ % concentrations at different time intervals in 3 subdivided experimental groups.

| Duration of Carotid Artery Ligation | COMPARED SUBDIVIDED GROUPS | | | | | |
|---|---|---|---|---|---|---|
| | Premannitol | | Mannitol-30 | | Mannitol-60 | |
| | W. Matter | Cortex | W. Matter | Cortex | W. Matter | Cortex |
| 3 hours (n: 8) | 81.5 ∓ 2.4 | 80.5 ∓ 2.6 | 78.4 ∓ 2.3 | 80.2 ∓ 3.9 | 76.3 ∓ 3.6 | 77.4 ∓ 1.8 |
| 6 hours (n: 8) | 76.3 ∓ 2.8 | 79.8 ∓ 1.3 | 76.3 ∓ 2.5 | 75.7 ∓ 2.7 | 74.7 ∓ 3.2 | 78.8 ∓ 1.8 |
| 10 hours (n: 8) | 75.9 ∓ 3.1 | 80.4 ∓ 2.1 | 74.3 ∓ 1.3 | 76.6 ∓ 1.7 | 72. ∓ 1.2 | 75.4 ∓ 1.6 |
| 12 hours (n: 8) | 75.1 ∓ 2.6 | 80.3 ∓ 2.2 | 76.6 ∓ 3.2 | 76.9 ∓ 2.8 | 77.9 ∓ 0 6 | 79.6 ∓ 1.6 |
| Kruskal Wallis' Variance Analysis (N: 32) | KW = 14.305 P < 0.01 | KW = 0.511 P > 0.05 | KW = 8.592 P < 0.05 | KW = 7.400 P > 0.05 | KW = 13.017 P < 0.01 | KW = 16.473 P < 0.01 |
| % $H_2O$ concentrations in NORMAL rats (n: 8): | | | W. MATTER: 78.09 ∓ 2.31 | | CORTEX: 79.39 ∓ 3.70 | |

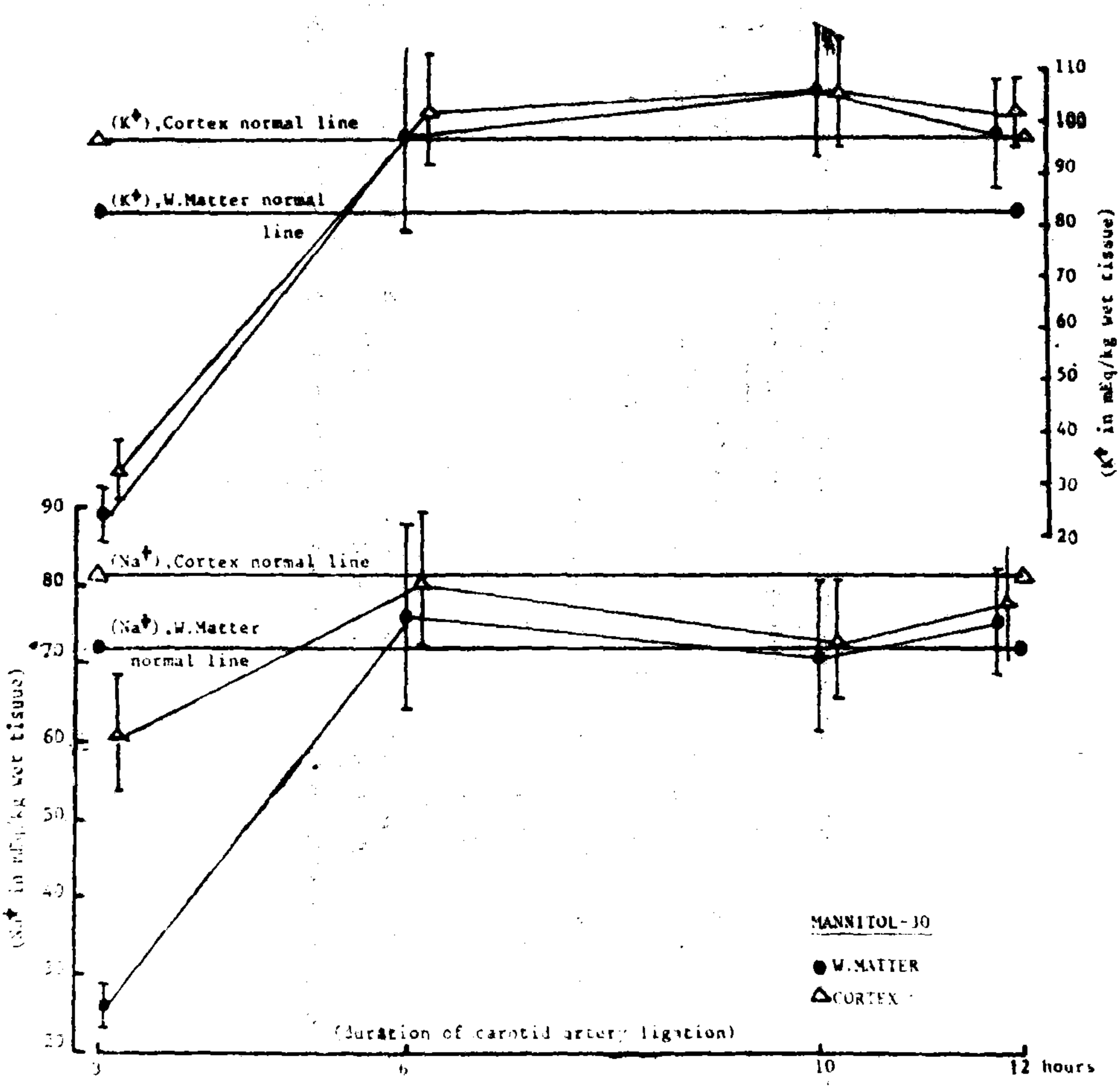


Figure 5. $H_2O$ concentrations in 3 subdivided groups, versus duration of the ligation.

Table 5. Comparison of the mean values of $Na^+$ concentrations of Cortex and W. Matter in the subdivided experimental and normal rat groups.

| Duration of Carotid Artery Ligation | Hemispheric Regions | COMPARED SUBDIVIDED AND NORMAL GROUPS | | | | | |
|---|---|---|---|---|---|---|---|
| | | Premannitol /Mannitol–30 | Premannitol /Mannitol–60 | Mannitol–30 /Mannitol–60 | Normal/Premannitol | Normal/Mannitol–30 | Normal/Mannitol–60 |
| 3 hours | Cortex | $t = 4{,}574$ $P < 0{,}01$ | $t = 6{,}164$ $P < 0{,}01$ | $t = 12{,}118$ $P < 0{,}01$ | $t = 8{,}198$ $P < 0{,}01$ | $t = 4{,}606$ $P < 0{,}01$ | $t = 16{,}612$ $P < 0{,}01$ |
| | W. Matter | $t = 7{,}877$ $P < 0{,}01$ | $t = 6{,}062$ $P < 0{,}01$ | $t = 2{,}346$ $P < 0{,}05$ | $t = 12{,}632$ $P < 0{,}01$ | $t = 17{,}065$ $P < 0{,}01$ | $t = 14{,}490$ $P < 0{,}01$ |
| 6 hours | Cortex | $t = 3{,}193$ $P < 0{,}02$ | $t = 2{,}625$ $P < 0{,}02$ | $t = 4{,}674$ $P < 0{,}01$ | $t = 3{,}067$ $P < 0{,}01$ | $t = 0{,}187$ $P > 0{,}05$ | $t = 4{,}401$ $P < 0{,}01$ |
| | W. Matter | $t = 3{,}375$ $P < 0{,}01$ | $t = 1{,}043$ $P > 0{,}05$ | $t = 2{,}873$ $P < 0{,}02$ | $t = 3{,}995$ $P < 0{,}01$ | $t = 0{,}620$ $P > 0{,}05$ | $t = 3{,}236$ $P < 0{,}01$ |
| 10 hours | Cortex | $t = 3{,}008$ $P < 0{,}01$ | $t = 2{,}351$ $P < 0{,}05$ | $t = 0{,}098$ $P > 0{,}05$ | $t = 1{,}017$ $P > 0{,}05$ | $t = 2{,}037$ $P > 0{,}05$ | $t = 1{,}516$ $P > 0{,}05$ |
| | W. Matter | $t = 0{,}886$ $P > 0{,}05$ | $t = 1{,}004$ $P > 0{,}05$ | $t = 0{,}144$ $P > 0{,}05$ | $t = 0{,}575$ $P > 0{,}05$ | $t = 0{,}412$ $P > 0{,}05$ | $t = 0{,}415$ $P > 0{,}05$ |
| 12 hours | Cortex | $t = 4{,}107$ $P < 0{,}01$ | $t = 0{,}438$ $P > 0{,}05$ | $t = 1{,}715$ $P > 0{,}05$ | $t = 2{,}285$ $P < 0{,}05$ | $t = 0{,}597$ $P > 0{,}05$ | $t = 1{,}056$ $P > 0{,}05$ |
| | W. Matter | $t = 1{,}042$ $P > 0{,}05$ | $t = 0{,}782$ $P > 0{,}05$ | $t = 1{,}537$ $P > 0{,}05$ | $t = 1{,}549$ $P > 0{,}05$ | $t = 0{,}650$ $P > 0{,}05$ | $t = 1{,}904$ $P > 0{,}05$ |

Table 6. Comparison of the mean values of $K^+$ concentrations of Cortex and W. Matter in the subdivided experimental and normal rat groups.

| Duration of Carotid Artery Ligation | Hemispheric Regions | COMPARED SUBDIVIDED AND NORMAL GROUPS | | | | | |
|---|---|---|---|---|---|---|---|
| | | Premannitol / Mannitol–30 | Premannitol / Mannitol–60 | Mannitol–30 / Mannitol–60 | Normal / Premannitol | Normal / Mannitol–30 | Normal / Mannitol–60 |
| 3 hours | Cortex | t = 6,407 P < 0,01 | t = 16,001 P < 0,01 | t = 10,907 P < 0,01 | t = 7,589 P < 0,01 | t = 2,352 P < 0,05 | t = 14,677 P < 0,01 |
| | W. Matter | t = 2,389 P < 0,05 | t = 1,684 P > 0,05 | t = 0,252 P > 0,05 | t = 12,813 P < 0,01 | t = 14,476 P < 0,01 | t = 13,375 P < 0,01 |
| 6 hours | Cortex | t = 1,305 P > 0,05 | t = 0,116 P > 0,05 | t = 2,015 P > 0,05 | t = 0,331 P > 0,05 | t = 0 ,870 P > 0,05 | t = 0,529 P > 0,05 |
| | W. Matter | t = 1,962 P > 0,05 | t = 1,202 P > 0,05 | t = 0,353 P > 0,05 | t = 0,451 P > 0,05 | t = 2,046 P > 0,05 | t = 1,351 P > 0,05 |
| 10 hours | Cortex | t = 0,742 P > 0,05 | t = 2,257 P < 0,05 | t = 2,414 P < 0,05 | t = 2,174 P < 0,05 | t = 1,628 P > 0,05 | t = 3,360 P < 0,01 |
| | W. Matter | t = 1,014 P > 0.05 | t = 1,419 P > 0,05 | t = 0,275 P < 0,05 | t = 1,761 P > 0,05 | t = 1,241 P > 0,05 | t = 4,651 P < 0,01 |
| 12 hours | Cortex | t = 1,879 P > 0,05 | t = 1,046 P > 0,05 | t = 0,099 P > 0,05 | t = 2,407 P < 0,05 | t = 1,328 P > 0,05 | t = 0,683 P > 0,05 |
| | W. Matter | t = 0,994 P > 0,05 | t = 1,938 P > 0,05 | t = 1,103 P > 0,05 | t = 2,070 P > 0,05 | t = 2,911 P < 0,02 | t = 3,499 P < 0,01 |

Table 7. Comparison of the mean values of $Na^+/K^+$ ratios in Cortex and W. Matter of the subdivided experimental and normal rat groups.

| Duration of Carotid Artery Ligation | Hemispheric Regions | COMPARED SUBDIVIDED AND NORMAL GROUPS | | | | | |
|---|---|---|---|---|---|---|---|
| | | Premannitol/ Mannitol–30 | Premannitol/ Mannitol–60 | Mannitol–30/ Mannitol–60 | Normal/ Premannitol | Normal/ Mannitol–30 | Normal/ Mannitol–60 |
| 3 hours | Cortex | t = 6,316 P < 0,01 | t = 1,340 P > 0,05 | t = 5,420 P < 0,01 | t = 1,266 P > 0,05 | t = 7,966 P < 0,01 | t = 3,026 P < 0,01 |
| | W. Matter | t = 1,385 P > 0,05 | t = 2,092 P > 0,05 | t = 1,299 P < 0,05 | t = 4,018 P < 0,01 | t = 3,649 P < 0,01 | t = 0,244 P > 0,05 |
| 6 hours | Cortex | t = 1,190 P > 0,05 | t = 1,333 P > 0,05 | t = 2,631 P < 0,02 | t = 2,222 P < 0,05 | t = 1,064 P > 0,05 | t = 3,658 P < 0,01 |
| | W. Matter | t = 1,622 P > 0,05 | t = 0,698 P > 0,05 | t = 2,000 P > 0,05 | t = 4,687 P < 0,01 | t = 2,571 P < 0,05 | t = 4,390 P < 0,01 |
| 10 hours | Cortex | t = 2,292 P < 0,05 | t = 3,250 P < 0,01 | t = 1,555 P > 0,05 | t = 0,142 P > 0,05 | t = 3,555 P < 0,01 | t = 4,600 P < 0,01 |
| | W. Matter | t = 3,913 P < 0,01 | t = 3,750 P < 0,01 | t = 0,370 P > 0,05 | t = 1,136 P < 0,05 | t = 5,937 P < 0,01 | t = 8,333 P < 0,01 |
| 12 hours | Cortex | t = 1,562 P > 0,05 | t = 0,204 P > 0,05 | t = 1,857 P > 0,05 | t = 1,163 P > 0,05 | t = 2,439 P < 0,05 | t = 0,395 P > 0,05 |
| | W. Matter | t = 1,194 P > 0,05 | t = 0,857 P > 0,05 | t = 0,364 P > 0,05 | t = 0,333 P > 0,05 | t = 2,439 P < 0,05 | t = 1,702 P > 0,05 |

Table 8. Comparison of the mean values of $H_2O$ % concentrations of Cortex and W. Matter in the subdivided experimental and normal rat groups.

| Duration of Carotid Artery Ligation | Hemispheric Regions | COMPARED SUBDIVIDED AND NORMAL GROUPS | | | | | |
|---|---|---|---|---|---|---|---|
| | | Premannitol/ Mannitol–30 | Premannitol/ Mannitol–60 | Mannitol–30/ Mannitol–60 | Normal/Premannitol | Normal/Mannitol–30 | Normal/Mannitol–60 |
| 3 hours | Cortex | t = 0,181 P > 0,05 | t = 2,773 P < 0,02 | t = 1,843 P > 0,05 | t = 0,694 P > 0,05 | t = 0,426 P > 0,05 | t = 1,368 P > 0,05 |
| | W. Matter | t = 2,638 P < 0,02 | t = 3,399 P < 0,01 | t = 1,224 P > 0,05 | t = 2,938 P < 0,01 | t = 0,269 P > 0,05 | t = 1,184 P > 0,05 |
| 6 hours | Cortex | t = 3,871 P < 0,01 | t = 1,274 P > 0,05 | t = 2,441 P < 0,05 | t = 0,296 P > 0,05 | t = 2,279 P < 0,05 | t = 0,405 P > 0,05 |
| | W. Matter | t = 0,000 P > 0,05 | t = 1,464 P > 0,05 | t = 1,391 P > 0,05 | t = 1,395 P > 0,05 | t = 1,488 P > 0,05 | t = 2,860 P < 0,02 |
| 10 hours | Cortex | t = 3,979 P < 0,01 | t = 5,359 P < 0,05 | t = 1,454 P > 0,05 | t = 0,671 P > 0,05 | t = 1,937 P > 0,05 | t = 2,800 P < 0,02 |
| | W. Matter | t = 1,347 P > 0,01 | t = 3,064 P < 0,01 | t = 3,2 P < 0,05 | t = 1,602 P > 0,05 | t = 4,909 P < 0,01 | t = 6,293 P < 0,01 |
| 12 hours | Cortex | t = 2,700 P < 0,02 | t = 0,728 P > 0,05 | t = 2,368 P < 0,05 | t = 0,598 P > 0,05 | t = 1,518 P > 0,05 | t = 0,147 P > 0,05 |
| | W. Matter | t = 1,029 P > 0,05 | t = 2,969 P < 0,01 | t = 1,129 P > 0,05 | t = 2,431 P < 0,05 | t = 1,068 P > 0,05 | t = 0,225 P > 0,05 |

## DISCUSSION

In this part of the study, the object was to investigate the effect of unilateral carotid artery ligation for different time intervals on the chemical alterations in water and electrolyte contents of the effected hemisphere. In a similar study (2) the neuronal alterations were studied and reported. As it is well known, cerebral collateral circulation in the rat is too rich, therefore it is not always possible to produce neuronal/chemical changes in the brain. Therefore our studies' aim was to look into if unilateral carotid ligation produces any chemical alteration, if so, also to study the effect of mannitol on those chemical alteriations. The threshold of ischemia producing neuronal and/or chemical alterations was experimentally shown that it may be different (11).

Chemical alterations shows some difference from the ischemic phase's point of view; that is, if it occured in the primary phase or secondary phase, chemical contents would be different (1, 9, 13, 15). Therefore, effectiveness of the agent in the ischemic conditions would depend on the time of administration of primary or secondary phase of the ischemic insult. When this is taken into consideration, mannitol should not be expected to effect the secondary complications, that is, mainly edema, because mannitol is thought to show its effect, as far as known, through the intact blood–brain barrier (BBB) (7, 8, 10, 14, 16, 17, 19, 20, 23).

The integrity of BBB could be tested using tracers, like Evans blue which was used in this experiment. In controls, no staining of the effected hemisphere was noticed but when we used in the mannitol treated rats, effected hemisphere was obviously stained.

The studies with mannitol showed conflicting results, both clinically and experimentally (2, 3, 4, 5, 6 , 8, 16, 17, 19, 23).

In this study, Na concentrations of both W. Matter and Cortex showed a statistically meaningful rise accordingly with ligation duration, which was reverse in the K concentaritons especially in first 3 hours of ligation. Again Na/K ratio was above 1 in the first 3 hours, returning back to normal by the 6. th hours of ligation duration. Apparently $H_2O$ contents was not effected by the carotid artery ligation in this experiment; on the other hand, mannitol did not show any statistical effect both on water and electrolyte concentrations either. Therefore, to be able to make any further comment on the effectiveness of mannitol it was necessary to carry out other studies (5, 6).

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